FACTORS AFFECTING ABSORPTION OF DRUGS

Factors Related to Drugs:

1. Lipid water solubility

Lipid water solubility coefficient is the ratio of dissolution of drug in lipid as compared to water. Greater the lipid water solubility coefficient, more is the lipid solubility of the drug and greater is the absorption. Less the coefficient, less is the lipid solubility and less is the absorption.

Water film exists on the membranes so part of the drugs must be water soluble to cross this water film

Drugs with benzene ring, hydrocarbon chain, steroid nucleus and halogen groups in their structures are lipid soluble.

2. Molecular size

Smaller the molecular size of the drug, rapid is the absorption. There exist different processes involved in absorption for different molecular sizes. Those with a large molecular size undergo endocytosis or facilitated diffusion, while those with smaller molecular sizes utilize aqueous diffusion or lipid channels.

3. Particle size

Particle may be composed either of a single molecule or more than hundred molecules. Larger is the particle size, slower will be the diffusion and absorption and vice versa.

4. Degree of Ionization

Different drugs are either acidic or basic and are present in ionized or unionized form, which is given by their pKa values. In the body, the ratio of the ionized and unionized forms depend on the pH of the medium. Acidic drugs are unionized in the acidic medium and basic drugs are unionized in the basic medium. Acidic drugs are better absorbed from the acidic compartment.

5. Physical Forms

Drugs may exist as solids, liquids or gases. Gases are rapidly absorbed than the liquids, while the liquids are rapidly absorbed than the solids. Thus the drugs in syrup or suspension form are rapidly absorbed than the tablets or capsules. Volatile gases used in general anesthesia are quickly absorbed through the pulmonary route.

6. Chemical Nature

Chemical nature is responsible for the selection of the route of administration of drug. Drugs that cannot be absorbed through the intestines are given by the parenteral route. Examples include heparin which is large molecular weight, and cannot be given orally. Simililarly, benzyl penicillin is degraded in the GIT, so is given parenterally.

Salt forms of drugs are better absorbed than the organic compounds when given orally. The organic compounds are given by routes other than the oral or enteral route.

Drugs in inorganic form are better absorbed than organic forms e.g. iron in Fe+2 is better absorbed than Fe+3, d-tubocurarine exists in ionized form and is a quaternary ammonium compound. Neostigmine is also a quaternary ammonium compound.

7. Dosage Forms
Dosage forms affect the rate and extent of absorption. A drug can be given in the form of tablets, capsules or transdermal packets. Injections may be aqueous or oily. This changes the rate of absorption. Examples include nitroglycerin which when given by sublingual route, disintegrates rapidly but stays for a shorter duration. When it is given orally, it disintegrates slowly and stays for longer duration. When given by transdermal route, the drug can cover an even longer duration.

a. Disintegration:
Disintegration is the breaking up of the dosage form into smaller particles. When rapid is the disintegration, rapid will be the absorption.

b. Dissolution:
After disintegration, the drug dissolves in the gastric juices, which is called dissolution. It is only then that the drug can be absorbed.

When these two processes occur rapidly, the rate of absorption increases.

8. Formulation
When the drugs are formed, apart from the active form some inert substances are included. These are the diluents, excipients and the binders. Normally they are inert, but if they interact, they can change the bioavailability. Examples include Na+ which can interact to decrease the absorption.

Atropine is required by some patients only in amounts of 0.2 to 0.6 mg.

9. Concentration
According to Fick’s law, higher the concentration more flux occurs across the membrane. The rate is less affected than the extent of absorption.

Factors Related to Body

1. Area of Absorptive Surface

Area of absorptive surface affects oral as well as other routes. Most of the drugs are given orally because of the large area of absorptive surface, so that greater absorption occurs. Intestinal resection decreases the surface area leading to a decreased absorption. Similarly, when the topically acting drugs are applied on a large surface area, they are better absorbed.

Organophosphate compounds are highly lipid soluble and poisoning can occur even by absorption through skin.

2. Vascularity

More the vascularity, more is the rate and extent of absorption and vice versa. In shock, blood supply to the GIT is less so the oral route of drug administration is affected. The blood flow to the peripheries is decreased, so absorption in those areas is diminished as well. Therefore, intravenous route is preferred in case of shock.

Vasoconstrictors decrease the blood supply of an area, thus are useful to restrict the local anesthesias so that they remain for a longer duration. Their wash away as well as their toxic effects are decreased in this way.

Massage in intramuscular injections improves vascular supply to enhance absorption.

3. pH

Acidic pH favors acidic drug absorption while basic pH is better for basic drugs.

4. Presence of other Substances

Foods or drugs may interact with the drugs to alter their rate of absorption. Especially for the drugs given orally, food can increase or decrease the absorption.

Antihyperlipidemic drugs like the statins are better absorbed when taken with the food.

Iron when given with milk has decreased absorption.

Vitamin C enhances the absorption of iron.

Phytates decrease iron absorption.

Milk decreases the absorption of tetracyclines.

Epinephrine when given with local anesthetics decreases their absorption.

Calcium salts when given with iron salts or tetracyclines interfere with their absorption

Aspirin is given with food while antibiotics are given in empty stomach. Liquid paraffin may affect drug absorption. Some acidic drugs bind with cholestyramine to from a complex which is not absorbed in GIT.

5. GI Mobility

GI mobility must be optimal for absorption of oral drugs. It should be neither increased nor decreased which may affect the rate or extent of absorption.

Different diseases or drugs may alter the mobility. Diarrhea causes rapid peristalsis, decreasing contact time and thus the extent of absorption is affected more. Constipation affects disintegration and dissolution so decreases motility.